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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/764,359	01/19/2001	Lola M. Reid	320727.50601	7133

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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/764,359	REID ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-9,12-21 and 23-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-4, 6-9, 12-21 and 23-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 5/12/06 was entered.

Claims 1, 3-4, 6-9, 12-21 and 23-34 are pending in the present application, and they are examined on the merits herein.

Remark

Should Applicants would like to request for a personal interview, please contact the examiner directly to arrange a convenient date and time for both Applicants and the examiner after receiving this Office action.

Upon further consideration and after consultation with Mr. Christopher Low, QAS (Quality assurance specialist) of Tech. Center 1600 on the issue of New Matter, the following New Matter rejection is applied.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4, 6-9, 12-21 and 23-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. ***This is a new ground of rejection with respect to the last Office Action.***

Claims 1, 3-4, 6-9 and 12-15 recite the limitation "**between about 2 hours and about 30 hours postmortem"** that also encompasses "**within about 2 hours and about six hours**" (claim 3) and "**within about 2 hours and about three hours**" (claim 4). Claims 16-21 and 23-32 recite the limitation "**between about 2 hours and 30 hours postmortem**". There is literally **no written support** for these specific ranges. The originally filed specification teaches that the tissues are harvested preferably within about 6 hrs after the donor's heartbeat ceased, preferably, within about three hours after the heartbeat ceased, more preferably, within about two hours after the heartbeat ceased and, most preferably, within about one hour after the heartbeat ceased, and the sooner the tissue is harvested after the donor's heartbeat ceased the better, including within about 45, 30, or 15 minutes after the donor's heartbeat ceased (page 5, lines 13-20). The originally filed specification also teaches to obtain organs or tissues within about twenty four hours or more after the heart beat ceased, and that it is preferable that the tissue is obtained within about sixteen hours after the heartbeat ceased, more preferably the tissue is obtained within about ten hours after the heartbeat ceased (page 6, lines 11-16); and livers obtained postmortem at different times but preferably within at least 24 hours, with a maximum of 30 hours (page 46, lines 11-12). However, none of these cited passages provides a written support for the specific ranges of a time period as claimed for obtaining or harvesting a tissue. Furthermore, the term "about 30 hours postmortem" encompasses a postmortem time beyond 30 hours, for example 30 hours

5 minutes, 30 hours 15 minutes, or even 31 hours; and the as-filed specification clearly teaches that livers obtained postmortem with a maximum 30 hours postmortem (page 46, lines 11-12). **Applicants are invited to point out the specific page and line numbers that support for the specific time ranges as claimed**. In the amendment filed on 6/28/05, Applicants cited page 46, lines 11-12 and page 31, lines 12-15 to provide support for the above limitation. However the examiner notes that the passage on page 46 lines 11-12 does not provide support for the specific time range as claimed (see above), and the passage on page 31, lines 12-15 merely states that "such livers are preferably isolated within the first 30 hours from heart arrest", and not the range between about 2 hours and about 30 hours postmortem or between about 2 hours and 30 hours postmortem.

Therefore, given the lack of guidance provided by the originally filed specification, it would appear that Applicants did not contemplate or have possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-4, 6-9, 12-21 and 23-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reid et al. (WO 95/13697; IDS) in view of Faris (U.S. 6,129,911 with the effective filing date of 7/10/1998; Cited previously) and Brasile (US 5,843,024). ***This is a new ground of rejection.***

Reid et al. discloses methods for isolating hepatoblasts comprising liver stem cells (pluripotent precursors) and committed precursors for either hepatocytes and bile duct cells using panning technologies and multiparametric FAC sorting from a single cell suspension of liver cells (see Summary of Invention). Reid et al. states "The methods of the invention have been developed using embryonic and neonatal livers from rats, however, the method of the invention offers a systemic approach to isolating hepatoblasts from any age from any species" (page 4, lines 6-10). This statement includes the isolation of hepatoblasts from adult liver (see page 43). Reid et al. also notes that hepatoblasts that are found in a high proportion of liver cells in early embryonic livers and in small number located periportally in adult livers (page 3, line 35 continues to line 1 of page 4). In the disclosed method (page 14, lines 9-15 for example), livers were dissected from donors, and placed into fresh ice-cold HBSS

(should be about 4^0C). Reid et al. also teaches that the tendency of isolated cells to aggregate is prevented by maintaining the cells at 4^0C and by removing calcium with EGTA (page 39, lines 24-33). Panned cells in the methods taught by Reid et al are sorted for multiple markers that distinguish subcategories of hepatic precursor cell populations, with the identified markers include: (a) the extent of granularity as measured by side scatter on fluorescence activated cell sorting, (b) the extent of autofluorescence and (c) the expression of a hepatic cell marker (page 12, lines 23-34).

Reid et al does not specifically teach a method of processing a non-fetal donor liver tissue or procuring liver progenitor cells from a liver tissue or processing a liver tissue obtained between about 2 hours and about 30 hours postmortem or between about 2 hours and 30 hours.

At the effective filing date of the present application (1/19/00), Faris already taught methods for isolating liver cell clusters comprising a liver stem cell and a hepatocyte, and a population of isolated liver stem cells from adult liver tissues from various species such as a mouse, a pig or a human; and that the liver tissues can be obtained from mammalian organ donors including deceased donors or cadavers (these donors do not have heart-beats, see col. 5, lines 3-25 and Summary of Invention).

Additionally, Brasile also disclosed a process for inducing repair of ischemically damaged organs and tissues (e.g., liver, kidney, heart) to the degree that impairment of function can be reversed and preventing further tissue damage during restoration of the circulation of the treated organ or tissue (see at least Summary of the Invention, col. 4, lines 29-32). In an exemplification, Brasile taught specifically a process used to

overcome the effects of warm ischemia in liver deprived of blood flow, and support a repair process to the degree that impairment of liver function can be reversed, comprising the steps of flushing and perfusing for approximately 2 hours in the resustation of most livers deprived of blood flow for between about 0.5 to 4 hours for resumption of organ function (example 9, cols. 17-18).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to modify the teachings of Reid et al. by also obtaining liver tissues from deceased donors or cadavers, including human deceased donors and cadavers, for the preparation of hepatoblast cell populations and that these liver tissues should be obtained as fresh as possible to avoid cell death in the harvested tissues caused by warm ischemia that ensues rapidly upon death of an organism, including liver tissues deprived of blood flow for between about 0.5 to 4 hours and subjected to the treatment of flushing and perfusion for approaximately 2 hours, in light of the teachings of Faris and Brasile.

An ordinary skilled artisan would have been motivated to carry out the above modifications because liver tissues from deceased donors and cadavers, particularly from humans, are available for obtaining an enriched population of liver stem and/or progenitor cells, and that liver tissues of at least up to 6 hours postmortem that have been subjected to the process taught by Brasile still retain organ function and without further tissue damage.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Reid et al, Farris, and

Brasile, coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The examiner further notes that the teachings of Reid et al. (WO 95/13697; IDS) are identical to those in U.S. Patent No. 6,069,005 and 6,242,252.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 3-4, 6-9, 12-21, 23-34 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 3-4, 6-9, 12-21, 23-34 of copending Application No. 10/620433. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2-4, 8-9, 12-21, 23-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,069,005 or claims 1-32 of US Patent No. 6,242,252 in view of Faris (U.S. 6,129,911 with the effective filing date of 7/10/1998; Cited previously) and Brasile (US 5,843,024).

The instant claims are directed to a method of processing non-fetal donor liver tissue to obtain an enriched population of progenitor cells, a method of procuring liver progenitor cells, a method of processing a liver tissue having at least one progenitor cell population or at least one diploid cell population, said methods comprise the step of providing non-fetal donor tissue obtained between about 2 hours and about 30 hours postmortem or harvesting a tissue from a donor having a non-beating heart between about 2 hours and 30 hours postmortem .

Claims 1-4 of U.S. Patent No. 6,069,005 are directed to a method of isolating hepatic progenitors from adult liver comprising the steps recited in claim 1.

Claims 1-32 of U.S. Patent No. 6,242,252 are drawn to a method of isolating hepatic progenitors from liver comprising the steps recited in either claim 1 or claim 14.

The claims of the present application differ from the claims of the U.S. Patent No. 6,069,005 or the claims of the U.S. Patent No. 6,242,252 in reciting specifically the step of providing non-fetal donor tissue obtained between about 2 hours and about 30 hours postmortem or harvesting a tissue from a donor having a non-beating heart between about 2 hours and 30 hours postmortem.

At the effective filing date of the present application (1/19/00), Faris already taught methods for isolating liver cell clusters comprising a liver stem cell and a hepatocyte, and a population of isolated liver stem cells from adult liver tissues from various species such as a mouse, a pig or a human; and that the liver tissues can be obtained from mammalian organ donors including deceased donors or cadavers (these donors do not have heart-beats, see col. 5, lines 3-25 and Summary of Invention).

Additionally, Brasile also disclosed a process for inducing repair of ischemically damaged organs and tissues (e.g., liver, kidney, heart) to the degree that impairment of function can be reversed and preventing further tissue damage during restoration of the circulation of the treated organ or tissue (see at least Summary of the Invention, col. 4, lines 29-32). In an exemplification, Brasile taught specifically a process used to overcome the effects of warm ischemia in liver deprived of blood flow, and support a repair process to the degree that impairment of liver function can be reversed,

comprising the steps of flushing and perfusing for approximately 2 hours in the resustation of most livers deprived of blood flow for between about 0.5 to 4 hours for resumption of organ function (example 9, cols. 17-18).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to modify claims 1-4 of U.S. Patent No. 6,069,005 or claims 1-32 of U.S. Patent No. 6,242,252 by also obtaining liver tissues from deceased donors or cadavers, including human deceased donors and cadavers, for the isolation of hepatic progenitors and that these liver tissues should be obtained as fresh as possible to avoid cell death in the harvested tissues caused by warm ischemia that ensues rapidly upon death of an organism, including liver tissues deprived of blood flow for between about 0.5 to 4 hours and subjected to the treatment of flushing and perfusion for approaximately 2 hours, in light of the teachings of Faris and Brasile.

An ordinary skilled artisan would have been motivated to carry out the above modifications because liver tissues from deceased donors and cadavers, particularly from humans, are available for obtaining an enriched population of liver stem and/or progenitor cells, and that liver tissues of at least up to 6 hours postmortem that have been subjected to the process taught by Brasile still retain organ function and without further tissue damage.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of either U.S. Patent No. 6,069,005 or U.S. Patent No. 6,242,252 with Farris, and Brasile, coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1, 3-4, 8-9, 12-21, 23-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 49, 51-53, 55-58, 60, 62-63 and 65-69 of copending Application No. 10/944,919 in view of Faris (U.S. 6,129,911 with the effective filing date of 7/10/1998; Cited previously) and Brasile (US 5,843,024).

The instant claims are directed to a method of processing non-fetal donor liver tissue to obtain an enriched population of progenitor cells, a method of procuring liver progenitor cells, a method of processing a liver tissue having at least one progenitor cell population or at least one diploid cell population, said methods comprise the step of providing non-fetal donor tissue obtained between about 2 hours and about 30 hours postmortem or harvesting a tissue from a donor having a non-beating heart between about 2 hours and 30 hours postmortem .

Claims of copending Application No. 10/944,919 are directed to a method of preparing a composition comprising a mixture of cells derived from adult human liver tissue, which mixture comprises an enriched population of human liver progenitors having the steps recited in claim 49 or a method of preparing a composition comprising an enriched population of human hepatic progenitors having the steps recited in claim 57.

The claims of the present application differ from the claims of copending Application No. 10/944,919 in reciting specifically the step of providing non-fetal donor tissue obtained between about 2 hours and about 30 hours postmortem or harvesting a tissue from a donor having a non-beating heart between about 2 hours and 30 hours postmortem.

At the effective filing date of the present application (1/19/00), Faris already taught methods for isolating liver cell clusters comprising a liver stem cell and a hepatocyte, and a population of isolated liver stem cells from adult liver tissues from various species such as a mouse, a pig or a human; and that the liver tissues can be obtained from mammalian organ donors including deceased donors or cadavers (these donors do not have heart-beats, see col. 5, lines 3-25 and Summary of Invention).

Additionally, Brasile also disclosed a process for inducing repair of ischemically damaged organs and tissues (e.g., liver, kidney, heart) to the degree that impairment of function can be reversed and preventing further tissue damage during restoration of the circulation of the treated organ or tissue (see at least Summary of the Invention, col. 4, lines 29-32). In an exemplification, Brasile taught specifically a process used to overcome the effects of warm ischemia in liver deprived of blood flow, and support a repair process to the degree that impairment of liver function can be reversed, comprising the steps of flushing and perfusing for approximately 2 hours in the resustation of most livers deprived of blood flow for between about 0.5 to 4 hours for resumption of organ function (example 9, cols. 17-18).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to modify claims of copending Application No. 10/944,919 by also obtaining liver tissues from deceased donors or cadavers, including human deceased donors and cadavers, for the preparation of an enriched population of human liver progenitors and that these liver tissues should be obtained as fresh as possible to avoid cell death in the harvested tissues caused by warm ischemia that ensues rapidly upon death of an organism, including liver tissues deprived of blood flow for between about 0.5 to 4 hours and subjected to the treatment of flushing and perfusion for approaximately 2 hours, in light of the teachings of Faris and Brasile.

An ordinary skilled artisan would have been motivated to carry out the above modifications because liver tissues from deceased donors and cadavers, particularly from humans, are available for obtaining an enriched population of liver stem and/or progenitor cells, and that liver tissues of at least up to 6 hours postmortem that have been subjected to the process taught by Brasile still retain organ function and without further tissue damage.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of the copending Application No. 10/944,919, Farris, and Brasile, coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Dave Nguyen, may be reached at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

QUANG NGUYEN, PH.D
PATENT EXAMINER